

## REMARKS/ARGUMENTS

Claims 1-7, 17-22, and 25-28 are currently under consideration in the application.

Applicants affirm their election of Group I without traverse, per the first paragraph of their Response of August 8, 2003. Claim 23 is canceled herewith.

Claims 1 and 7 stand rejected over de Macario in view of Cole. These claims are drawn to creating a concentration gradient across a set of containers by differential diffusion during the course of contacting the containers with a liquid.

Claim 18 stands rejected as indefinite, while claim 25 stand rejected as anticipated by Davis. Claims 17-18, 21-23, 25, and 27-28 stand rejected as anticipated by de Macario. Claims 19-20 and 26 stand rejected over de Macario in view of Davis, while claim 26 stands rejected additionally on grounds of obvious-type double patenting.

Correction of a typographical error made in typesetting paragraph [0104] of the published application is requested, as set out above.

### **Differential Diffusion Creating a Concentration Gradient**

Claims 1 and 7 relate to a method whereby the containers of an integral structure, having already been filled with a first liquid, are then filled

- by contact with a second liquid
- such that the degree of diffusion of a specific substance varies with position among the containers, thereby creating a gradient of that substance with respect to position of the container within the structure.

De Macario has neither of these. Cole has a set of samples characterized by a concentration gradient of antibiotic materials, but suggests *neither*

- contacting containers with a liquid as a means of filling the containers, nor

· using differential diffusion so that the contents of the containers exhibit a gradient with respect to a specified chemical species.

The Examiner's attention is directed to pp. 28-30 for a detailed discussion of various examples of how the claimed method may be accomplished in accordance with the present invention. There is, however, no teaching or suggestion of any such method in either De Macario or Cole.

Claims 1 and 7 are therefore patentable over the cited references, and withdrawal of the rejection is requested.

### **Stacking**

Claims 17-20 are drawn to methods for loading a liquid into a plurality of through-holes.

Examiner's point regarding the infelicity of language of claim 18 (invoking gaps in a 'continuous channel') having been considered, claim 17 has been amended to require that a continuous *column* of fluid is required to be formed, even though, as in the embodiment of claim 18, the channel itself may be discontinuous, such as in cases where the stacked platens are separated by an air gap. Filling a stack of arrays is described in par. 101 of the Application, the continuity of the column of liquid is described there and at various other places in the application, for example, at par. 104, now amended to read: "The volume of liquid withdrawn into each syringe preferably equals the volume of liquid in a column of aligned through-holes in the array stack." Thus, the rejection of claim 18 for indefiniteness has been overcome.

The cited passage of de Macario is unclear and not enabling, but, no reasonable reading relates to loading a liquid into a plurality of through-holes by virtue of stacking since the through-holes of de Macario are already loaded. Here's what de Macario says:

The small separation between plates **130** and **134** enables the liquid sample placed on retaining element **132** (or on retaining element **136**) or on retaining element **132'**, to form a liquid bridge suspended between the retaining elements of the adjacent plates. (De Macario, col. 10, lines 32-36)

Thus, according to de Macario, each of the holes ('retaining elements') is filled separately, then, while it is unclear how that serves 'to form a liquid bridge,' the plates are inserted into parallel vertical slots. Perhaps the filled plates are contacted with each other and then separated? In any event, the claimed method step of transferring a liquid to form a continuous column is not suggested. Thus, none of claims 17 and the claims dependent therefrom, claims 18-20, can have been anticipated by de Macario. Nor does Davis provide the missing teaching, thus each of claims 17-20 is patentable over de Macario, alone or in combination with Davis.

### **Mixing**

Claims 21, 22, 27 and 28 are drawn to a method of mixing liquids contained in two platens by stacking them to allow diffusion between connecting through-holes. There is no such teaching in de Macario. Indeed, de Macario teaches that mixing is achieved by adding reagents and samples separately to the holes of a single platen, there being no suggestion of any parallelism that might be achieved by aligning corresponding holes. Nor does Davis supply the missing teaching, thus claims 21, 22, 27, and 28 are patentable over de Macario and Davis, alone or in combination.

### **Diffusion of Light by an Array of Liquid Microlenses**

As there is no teaching in the cited references of illuminating a microchannel plate filled with liquid in order to diffuse the light, as described in the application at page 36, lines 18-21, claim 25 is deemed patentable over the art of record.

### **Perforated Platen Permitting Retention of Distinct Samples**

Claim 26 has been amended to clarify that the claimed structural requirements permit the retention in adjacent through-holes of distinct samples, without capillary outmigration ("...different chemical species may be loaded into different through-holes of the array" – Application, p. 8, lines 9-10). There is no suggestion to combine Davis with de Macario in this regard, as has been discussed in the prosecution history of the related parent applications, U.S.S.N. 09/225,583 and 09/710,082. Davis teaches that only a single liquid may be loaded into a mesh. Consequently, claim 26 is patentable over the art of record.

Appl. No. 09/850,123  
Amdt. Dated January 9, 2004  
Reply to Office Action of October 10, 2003

Claim 26 has been amended, additionally, to recite a through-hole diameter less than 400 micrometers. (Application, p. 9, line 12)

Finally, the distinct liquids contained within adjacent through-holes have not previously been claimed, so that withdrawal of the obviousness-type double-patenting rejection and allowance of claim 26 are requested.

If the Examiner has any outstanding questions, he is invited to call Applicants' undersigned representative at 617-443-9292.

Respectfully submitted,



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